45. (New) The method of claim 19, wherein A and A_1 are L- or D- isomers of naturally occurring amino acid residues.

46. (New) The pharmaceutical preparation of claim 36, wherein m in Formula II is zero.

47. (New) The pharmaceutical preparation of claim 46, wherein A_1 is selected from the group consisting of valine, lysine, proline and alanine.

C4

48. (New) The pharmaceutical preparation of claim 36, wherein A and A_1 are L- or D- isomers of naturally occurring amino acid residues.

49. (New) The pharmaceutical preparation of claim 37, wherein m in Formula II is zero.

50. (New) The pharmaceutical preparation of claim 49, wherein A_1 is selected from the group consisting of valine, lysine, proline, and alanine.

51. (New) The pharmaceutical preparation of claim 37, wherein A and A_1 are L- or D- isomers of naturally occurring amino acid residues.

Remarks

Claims 1, 19, 36 and 37 have been amended to recite Formula II compounds that comprise L- and D- amino acid residues, as described in the provisional patent application to which priority is claimed. Support for these amendments can be found in the provisional patent application on page 2, lines 20-26, page 3, lines 1-3, and page 13, lines 22-25, combined with the incorporation by reference found on page 1, lines 7-9 of the instant application.

The Examiner has indicated that claims 3 and 8 would be allowable if re-written in independent form. Applicants have done so, but have introduced these claims as new claims 38 and 39.

New claims 40-51 have been introduced. Support for these claims can be found throughout the specification and in the claims as filed. Support for claims 40, 43, 46 and 49 can be found in claims 1, 19, 36 and 37. Support for claims 41, 44, 47 and 50 can be found in the

specification on page 3, lines 14-18 and 20, and in the provisional specification on page 3, line 15 and page 12, lines 17-19. Support for claims 42, 45, 48 and 51 can be found throughout the specification and particularly on page 12, lines 16-19, and in the provisional specification on page 13, lines 22-25.

If the addition of these claims necessitates an additional claim fee, the Examiner is authorized to charge any such small entity fee to the Deposit Account of the undersigned as indicated on the transmittal.

Applicants reserve the right to pursue the subject matter of the originally filed claims in a continuing application.

No new matter has been added.

Entitlement of Priority for Amendments to Claims 1, 19, 36 and 37

The Examiner states that claims 1-8, 11-17, 19, 31, 36 and 37 are not entitled to the benefit of the filing date of provisional application 60/135,861 because the provisional application does not disclose the compounds of Formula II, nor does it disclose compounds in which A and A_1 can be any L- or D- amino acid. As a result of this, the Examiner now asserts PCT Patent Application 00/10549 against the instant claims as prior art under 35 USC 102(a).

Applicants have amended claims 1, 19, 36 and 37 to recite Formula II as found in the provisional application, based on an incorporation by reference asserted on page 1, lines 7-9 of the instant application. The Examiner states that claim 18, which recites an agent that is ValboroPro, is entitled to the filing date of the provisional application.

Applicants have further amended claims 1, 19, 36 and 37 to recite that A and A_1 of Formula II are L- or D- amino acid residues. The Examiner acknowledges that the provisional application supports L- amino acids. Page 14, lines 22-25 of the provisional application teaches that the invention embraces the use of D- amino acids. The non-provisional application has a similar teaching.

Accordingly, the claims as now amended are entitled to a priority filing date of the provisional application, and PCT Patent Application 00/10549 is no longer a prior art against the pending claims.

Provisional Non-Statutory Double Patenting Rejection

Claims 1, 2, 11-19, 31, 36 and 37 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claim 1-21 of copending Application No. 09/744,658 in view of O'Reilly et al. and Brooks et al.

Applicants' representative previously discussed this rejection with the Examiner and stated that the claims of Application No. 09/744,658 would be amended in order to overcome the double patenting rejection. As this is a provisional rejection, Applicants propose to amend the claims of Application No. 09/744,658 once the claims in the instant application are allowed.

Showing of Common Ownership

The Examiner requests a showing under 37 CFR 1.78(c) and 35 USC §132 that the instant application and Application 09/744,658 were commonly owned at the time the instant invention was made. A statement asserting that the applications were commonly owned at the time the instant invention was made is being prepared and will be forwarded to the Examiner once executed by the common assignee, Point Therapeutics, Inc.

Rejection under 35 U.S.C. 103(a)

In view of WO 00/10549 and et al. (USP 5,854,205) or Brooks et al. (USP 5,753,23

Claims 1, 2, 11-17, 19, 31, 36 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over WO 00/10549, in view of O'Reilly et al. (USP 5,854,205) or Brooks et al. (USP 5,753,230).

Applicants have amended claims 1, 19, 36 and 37 to recite agents of Formula II as supported in the provisional application to which priority is claimed. The provisional application supports both L- and D- amino acid residues. (See page 13, lines 22-25 of provisional application 60/135,861.) Accordingly, WO 00/10549 is removed as a prior art reference, and the combination relied upon by the Examiner does not render the pending claims obvious.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C 103(a) as being obvious over WO 00/10549 in view of O'Reilly et al. and Brooks et al.

In view of WO95/15309 and O'Reilly et al. (USP 5,854,205) or Brooks et al. (USP 5,753,230)

Claims 1, 2, 4-7, 11-17, 31, 36 and 37 are rejected under 35 U.S.C. 103(a) as being obvious over WO95/15309, in view of O'Reilly et al. (USP 5,854,205) or Brooks et al. (USP 5,753,230).

Applicants have amended claims 1, 19, 36 and 37 to recite agents of Formula II as supported in the provisional application, and to include the limitation that A and A_1 in Formula II are L- or D- amino acid residues.

WO95/15309 teaches DP-IV inhibitors, and categorizes these into three groups. WO95/15309 contemplates that "potent inhibitors of DP-IV may be useful as drugs for the treatment of human disease" including in the prevention of metastases. However, the reference draws a distinction between the groups of compounds, particularly with regard to their structure and their proposed therapeutic utility. For example, the reference teaches that compounds of Group I "could be useful as immunosuppressants; anti-HIV infectivity agents; agents to suppress release of certain cytokines ... from activated T cells." The reference further teaches that compounds of Group II could have the same uses as Group I compounds and in addition could block the interaction of DP-IV with tumour cell surface fibronectin or with any other ligand important for tumour cell adhesion. Accordingly, the broad suggestion that DP-IV inhibitors are useful in preventing metastasis must be limited by the qualification that Group II, but not Group I compounds, could have this utility. As a result, the reference cannot reasonably be read as teaching that Group I compounds are useful in proliferative disorders such as those of the pending claims.

The Examiner has cited the reference for its teaching of Group I compounds (specifically those numbered 41-45 on pages 17 and 18). As stated above, however, the reference does not teach that Formula I compounds are useful in proliferative disorders, but rather teaches that Group II compounds are useful in these disorders. The combination with O'Reilly et al. or Brooks et al. does not cure the deficiency in the teaching of WO95/15309. Accordingly, the combination does not render obvious the claimed invention at least because there is no motivation to combine Group I compounds of WO95/15309 with the teachings of the secondary references.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims under 35 U.S.C 103(a) as being obvious over WO95/15309 in view of O'Reilly et al. or Brooks et al.

In view of WO95/15309, O'Reilly et al. (USP 5,854,205) or Brooks et al. (USP 5,753,230), and WO00/10539

Claim 19 is rejected under 35 U.S.C. 103(a) as being obvious over WO95/15309, in view of O'Reilly et al. (USP 5,854,205) or Brooks et al. (USP 5,753,230), in further view of WO 00/10539.

WO00/10539 has been removed as a prior art reference. Accordingly, this rejection is based on the combination of WO95/15309 in view of O'Reilly et al. or Brooks et al. which has been argued above.

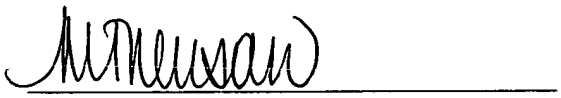
In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims under 35 U.S.C 103(a) as being obvious over WO95/15309 in view of O'Reilly et al. or Brooks et al., and in further view of WO00/10539.

Summary

Applicants believe that each of the pending claims is in condition for allowance. Applicants respectfully request that the Examiner telephone Applicants' representative in the event that the claims are not found to be in condition for allowance.

If the Examiner has any questions and believes that a telephone conference with Applicants' representative would prove helpful in expediting the prosecution of this application, the Examiner is urged to call the undersigned at (617) 720-3500 (extension 266).

Respectfully Submitted,



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Docket No.: I00248.70012.US
Date: November 7, 2002
X11/07/02

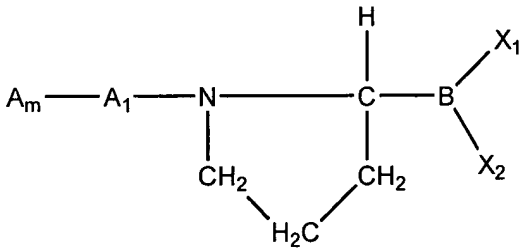
APPENDIX A

MARKED-UP CLAIMS

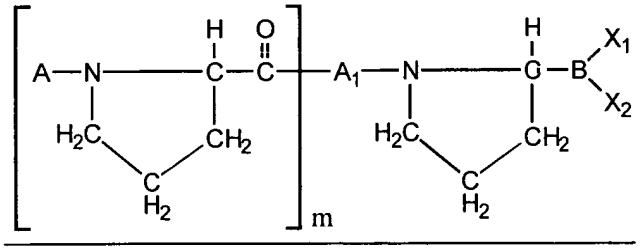
Please amend the claims as follows:

1. (Twice Amended) A method for treating a subject having a condition characterized by an abnormal mammalian cell proliferation, comprising:

administering to a subject in need of such treatment, a compound selected from the group consisting of an anti-angiogenic compound and an anti-cancer compound, and an agent, in an amount effective to inhibit the proliferation, wherein the agent is a compound of Formula II [



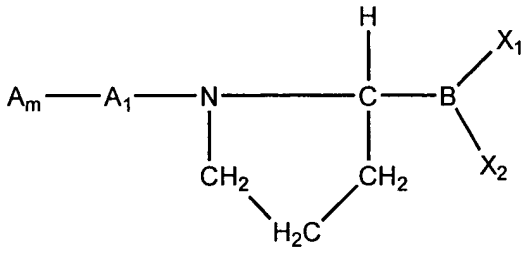
wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; and each X_1 and X_2 is independently a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH]



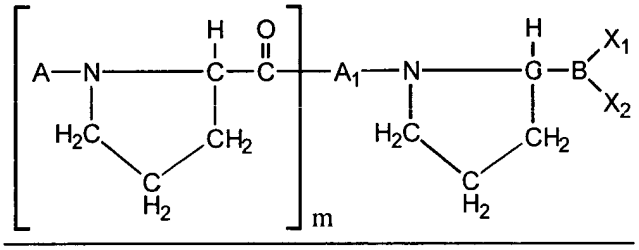
wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; A in each repeating bracketed unit can be a different amino acid residue; the C bonded to B is in the L-configuration; the bonds between A and N, A_1 and C, and between A_1 and N are peptide bonds; and each X_1 and X_2 is, independently, a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH.

19. (Twice Amended) A method for inhibiting angiogenesis in a subject having a condition characterized by abnormal mammalian cell proliferation comprising:

administering to a subject in need of such treatment, a compound selected from the group consisting of an anti-angiogenic compound and an anti-cancer compound, and an agent, in an amount effective to inhibit angiogenesis in an abnormal proliferative cell mass, wherein the agent is a compound of Formula II [



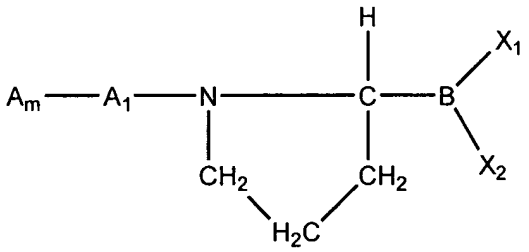
wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; and each X_1 and X_2 is independently a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH].



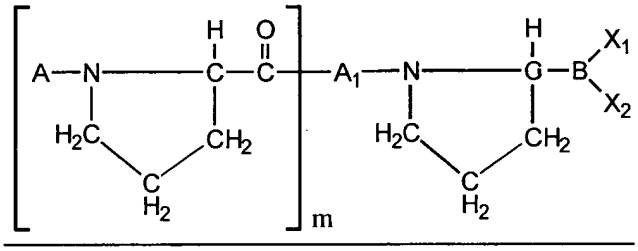
wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; A in each repeating bracketed unit can be a different amino acid residue; the C bonded to B is in the L-configuration; the bonds between A and N, A_1 and C, and between A_1 and N are peptide bonds; and each X_1 and X_2 is, independently, a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH.

36. (Twice Amended) A pharmaceutical preparation comprising:

an agent of Formula II [



wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; and each X_1 and X_2 is independently a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH,]



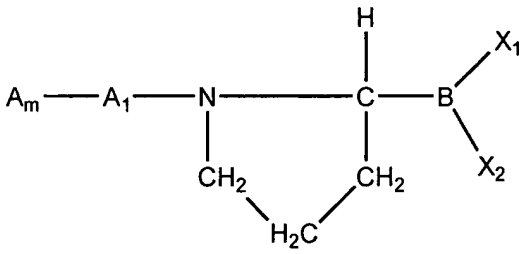
wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; A in each repeating bracketed unit can be a different amino acid residue; the C bonded to B is in the L-configuration; the bonds between A and N, A_1 and C, and between A_1 and N are peptide bonds; and each X_1 and X_2 is, independently, a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH,

at least one other anti-cancer compound, and

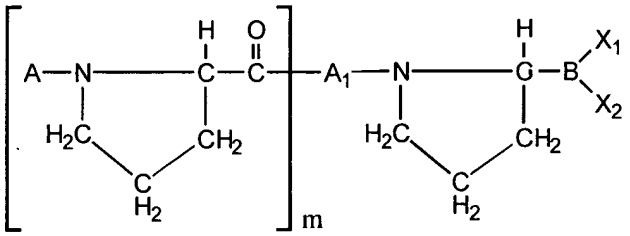
a pharmaceutically acceptable carrier.

37. (Twice Amended) A pharmaceutical preparation comprising:

an agent of Formula II [



wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; and each X_1 and X_2 is independently a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH ,]



wherein m is an integer between 0 and 10, inclusive; A and A_1 are L- or D-amino acid residues; A in each repeating bracketed unit can be a different amino acid residue; the C bonded to B is in the L-configuration; the bonds between A and N, A_1 and C, and between A_1 and N are peptide bonds; and each X_1 and X_2 is, independently, a hydroxyl group or a group capable of being hydrolyzed to a hydroxyl group in aqueous solution at physiological pH,

at least one other anti-angiogenic compound, and

a pharmaceutically acceptable carrier.